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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/782,269	02/18/2004	Viorica Lopez-Avila	10031188-1	4020

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EXAMINER

LUM, LEON YUN BON

ART UNIT

PAPER NUMBER

1641

DATE MAILED: 03/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/782,269	LOPEZ-AVILA ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Leon Y. Lum	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 29 December 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-5,8-30 and 37-44 is/are pending in the application.
- 4a) Of the above claim(s) 19-27 and 38-44 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5,8-18,28-30 and 37 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

## DETAILED ACTION

1. The amendment filed December 29, 2005 is acknowledged and has been entered.

### ***Claim Rejections - 35 USC § 102***

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-5, 10-15, 17-18, and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Little et al (US 6,387,628 B1).

Little et al reference teaches the immobilization of a polypeptide of interest to a solid support (i.e. planar substrate having a surface) using a pin tool in an array (i.e. contacting a sample), wherein the pin tool has antibodies attached to each pin tip to capture polypeptides (i.e. array of features containing a capture agent that specifically binds to an analyte), and wherein the pin conformation can include nanowells (i.e. each of said features is surrounded by a fluid retaining structure). See column 50, lines 1-55. In addition, Little et al teach that a pin tool can be washed with ammonium citrate to condition the polypeptide prior to addition of matrix for identity determination by mass spectrometry, wherein the mass spectrometry can be MALDI (i.e. processing any

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analytes bound to said capture agents for MALDI analysis). See column 51, lines 2-7 and column 54, lines 49-51. Little et al also teach the detection of different polypeptides. See column 11, lines 22-35. Since different polypeptides are detected, it is necessarily required that the pin tools contain more than one type of functional group to immobilize the different polypeptides (i.e. array of features containing different capture agents). Furthermore, Little et al teach that polypeptides can be released or transferred from the pins prior to analysis or cleaved from the pins into a nanowell on a chip prior to addition of matrix, and that the pin tool can pass prepared polypeptide arrays to a plate assembly that disposes the arrays for analysis by mass spectrometry (i.e. transferring any processed products from step (b) to features of a MALDI sample plate, to prepare said MALDI sample plate). See column 50, lines 60-64; column 51, lines 12-14; and column 52, lines 17-21.

With regards to claims 2-5, Little et al teach that the pins include a jet assembly (i.e. pulse-jet and contact fluid delivery device) and are used to immobilize a polypeptide of interest and can transfer polypeptides from the pins prior to analysis (i.e. employed in steps (a) and (c)) and can be washed to condition the polypeptide prior to addition of matrix (i.e. employed in step (b)), as stated above. See column 50, lines 2-13; column 51, lines 2-7 and 12-14; column 52, line 5; and column 54, lines 49-51.

With regards to claims 10-11, Little et al teach that the pins can have antibodies specific for a target polypeptide attached thereto (i.e. capture agents are antibodies; comprise an affinity label). See column 50, lines 34-38.

With regards to claim 12, Little et al teach that sample is analyzed by MALDI mass spectrometry (i.e. evaluating said transferred products using a MALDI mass spectrometer to gather data on and assess said sample), as stated above. See column 54, lines 49-51.

With regards to claims 13 and 17, Little et al reference teaches MALDI mass spectrometric analysis to provide accurate measurement of molecular weight (i.e. determining molecular weights; quantitative). See column 4, lines 2-18, especially lines 2-5 and 16-17.

With regards to claim 14, Little et al teach that identification of the polypeptide is effected by comparison with a reference polypeptide, wherein the molecular mass of peptide fragments of the target polypeptide is compared with the molecular mass of peptide fragments of a corresponding known polypeptide (i.e. comparing said determined molecular weights to molecular weights of pre-determined analytes). See column 57, lines 30-33 and column 58, lines 10-12.

With regards to claim 15, Little et al teach that the masses of peptide fragments of a corresponding known polypeptide can be obtained from a database of polypeptide sequence information (i.e. wherein said molecular weights for said pre-determined analytes are in a database). See column 58, lines 12-15 and 19-22.

With regards to claim 18, Little et al teach that the masses of peptide fragments of a corresponding known polypeptide can be determined in parallel reaction with the target polypeptide, wherein the corresponding known polypeptide is also contacted with

the agent (i.e. assessing the formation of capture agent/analyte complexes relative to the formation of control capture agent/analyte complexes). See column 58, lines 12-16.

***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

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consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Little et al (US 6,387,628 B1) in view of Marshall (US 5,236,826).

Little et al reference has been disclosed above, but fails to teach the step of separating analytes that are bound to said capture agents from those that are not bound to said capture agents.

Marshall reference teaches washing bound and unbound material components, in order to reduce the amount of background noise present by unbound signal generating material remaining in the zone of measurement. See column 5, line 60 to column 6, line 7. Marshall reference also teaches that the components are in a solid phase immunoassay. See column 4, lines 4-8.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Little et al with the step of washing bound and unbound material components, as taught by Marshall, in order to reduce the amount of background noise present by unbound signal generating material remaining in the nanowells of the pin array. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in washing away unbound material, as taught by Marshall, in the method of Little et al, since Little et al teach a solid phase immunoassay, and the washing step taught by Marshall is performed on a solid phase immunoassay.

8. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Little et al (US 6,387,628 B1) in view of Krantz et al (US 5,840,733).

Little et al reference has been disclosed above, but fails to teach the step of drying said transferred products on said MALDI sample plate.

Krantz et al reference teaches that samples for MALDI-MS were mixed on an analysis plate with a matrix and then dried, in order to allow for crystallization and insertion into an instrument for laser ionization. See column 12, lines 44-49.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Little et al with the step wherein samples in the nanowells of the pin array were mixed on an analysis plate with a matrix and then dried, as taught by Krantz et al, in order to allow for crystallization and insertion into an instrument for laser ionization to perform MALDI-MS. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in drying the matrix mixture, as taught by Krantz et al, in the method of Little et al, since Little et al teach mixing polypeptide sample with matrix prior to MALDI mass spectrometry, and the drying step taught by Krantz et al is also performed prior to MALDI mass spectrometry.

9. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Little et al (US 6,387,628 B1) in view of El Shami et al (US 6,525,187 B1).



Little et al reference has been disclosed above, but fails to teach that said evaluating is determining amounts of said analytes bound to said capture agents.

El Shami et al reference teaches determining a test amount of an analyte, in order to compare an amount of an analyte in a subject sample to that of a normal amount of analyte from a healthy individual, wherein the analyte is a protein and is detected using MALDI mass spectrometry. See column 13, lines 25-35 and column 43, lines 30-38.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Little et al with the step of determining a test amount of an analyte, as taught by EL Shami et al, in order to compare an amount of an analyte in a subject sample applied to the pin array to that of a normal amount of analyte from a healthy individual, wherein the analyte is a protein and is detected using MALDI mass spectrometry. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in determining the amount of analyte, as taught by El Shami et al, in the method of Little et al, since both Little et al and El Shami et al utilize MALDI mass spectrometry for detecting analytes.

10. Claims 28-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Little et al (US 6,387,628 B1) in view of Sugiyama (US 6,828,421 B1).

Little et al reference has been disclosed, but fails to teach the step of transmitting data from a first location to a second location, wherein the second location is a remote location, and receiving a transmitted result of a reading of an array.

Sugiyama reference teaches the step of transmitting data in the form of email or posted on a website, wherein the data includes molecular weight information, in order to communicate information to other researchers in a different country. See column 45, line 50 to column 46, line 16.

It would have been obvious to one ordinary skill in the art at the time of the invention to modify the method of Little et al with of transmitting data in the form of email or posted on a website, wherein the data includes molecular weight information, as taught by Sugiyama, in order to communicate analysis information on samples in the pin array to other researchers in a different country. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in transmitting data by email or internet posting, as taught by Sugiyama, in the method of Little et al, since Little et al teach the identification of target analyte by determining the analyte's molecular weight, and the data transmitted by Sugiyama can include molecular weight information.

### ***Double Patenting***

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir.

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1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1-6, 8-18, 28-30, and 37 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of copending Application No. 11/001493. Although the conflicting claims are not identical, they are not patentably distinct from each other because they both claim the same subject matter.

The instant application recites a method for preparing a MALDI sample plate, comprising contacting a sample with an array of features, wherein said array comprises a planar substrate having a surface on which said features are positioned and each of said features is surrounded by a fluid retaining structure containing a capture agent that specifically binds to an analyte, processing any analytes bound to said capture agents for MALDI analysis, and transferring any processed analytes to individual features of a MALDI sample plate each surrounded by a fluid retaining structure, to prepare said MALDI sample plate.

The copending application teaches the same method steps of the instant application, but does not specifically teach a planar substrate with features surrounded

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by a fluid retaining structure, and the step of processing analytes bound to said capture agents for MALDI analysis.

However, the copending application does teach a plurality of wells of a multi-well sample plate and the step of contacting said washed matrix with a MALDI cleavage agent to produce a solution containing cleavage-agent treated analytes.

It would have been obvious to one of ordinary skill in the art at the time of the invention to recognize that a plurality of wells in a multi-well sample plate is one specific example of the broader claimed limitation of a planar substrate with features surrounded by a fluid retaining structure. In addition, it would have been obvious to one of ordinary skill in the art at the time of the invention to also recognize that the step of producing a solution of cleavage-agent treated analytes for MALDI analysis is one example of the broader claimed limitation of processing analytes for MALDI analysis. Therefore, since the copending application teaches narrower and more specific limitations that meet the claimed invention, the instant application is not patentable over the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### ***Response to Arguments***

13. On pages 7-9 of the Response, Applicants traverse the rejections of the pending claims as either anticipated by Little et al (US 6,387,628) or as obvious over Little et al

in view of a variety of secondary references. Applicants specifically argue Little et al do not teach the claimed "planar substrate" and that the other references do not remedy the alleged failings of Little et al.

On page 7 of the Response, Applicants recognize that the pin array of Little et al is applied to teach the claimed "array of features" which requires a planar substrate having a surface on which said features are positioned. However, Applicants submit that "A pin array is not a planar substrate having a surface on which said features are positioned." See page 7, 4<sup>th</sup> paragraph under section titled "Rejection under 35 U.S.C. 102". Applicants do not further embellish why the pin array is not considered as a planar substrate having a surface on which features can be positioned.

Applicants' arguments have been fully considered, but are not persuasive. Given Applicants' statements, it is assumed that Applicants consider their invention to comprise a flat surface, of which Applicants argue a pin array supposedly does not have. The support provided for a flat surface is disclosed in the specification as plates that have wells, walls, or other three-dimension structures including microtiter plates. See page 12, section 042. However, these plates are only presented in the form of **examples**, which do not limit the claimed substrate to the examples disclosed. There is no actual stated physical limitation on the form a substrate takes. The only requirement is that the substrate comprise two embodiments: (1) a *surface* that can support features and (2) the features are surrounded by a *fluid retaining structure*. Therefore, any substrate in the prior art that teaches these two embodiments anticipates the claimed substrate.

With respect to the first embodiment of the substrate, the specification does not define the term "surface", nor recite any limitations on what the surface can comprise. By providing the example of microtiter plates as the substrate, it is assumed that Applicants consider the array of well bottoms as the surface. However, the lack of a definition or limitation in the specification on what the "surface" can comprise allows any flat substrate with an array of two or three-dimensional structures accommodating features to read on the claimed surface. The pin array of Little et al is disclosed as an array of pins connected to a mounting plate, wherein the pins comprise nanowells at the tip for holding biological capture agents. See column 50, lines 39-55. The mounting plate is considered to teach the "planar substrate", the pins as the "surface", and the nanowells as the "fluid retaining structure". While this arrangement is different from the microplates of Applicants' examples in the specification, it falls wholly within the scope of the claimed invention since the specific embodiments claimed, especially the "surface", have not been limited by any means in the specification.

Applicants' arguments are therefore not considered to be persuasive, and the rejections made in the previous Office Action have been maintained.

### ***Conclusion***

14. No claims are allowed.

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on weekdays from 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.


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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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3/14/06